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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,902	01/09/2006	Roland Schule	033-004	5822

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CERMAK KENEALY VAIDYA & NAKAJIMA LLP
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EXAMINER

HIRIYANNA, KELAGINAMANE T

ART UNIT	PAPER NUMBER
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1633

NOTIFICATION DATE	DELIVERY MODE
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01/28/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/561,902	Applicant(s) SCHULE ET AL.	
	Examiner KELAGINAMANE T. HIRIYANNA	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 October 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) 7-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's response filed on 10/30/2008 in response to office action mailed on 04/30/008 has been acknowledged.

Claims 1-5 are amended.

Claims 1-6 are pending and are examined in this office action.

*Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is **571-273-8300**.*

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Withdrawn: Claim objections of record set forth in the office action mailed on 04/30/008 is withdrawn in view of Applicants appropriate amendments to claims filed in the Applicants response of 10/30/2008.

Withdrawn: Claims 1-6 rejection of record set forth in the office action mailed on 04/30/008 under 35 U.S.C. 112, first paragraph (enablement) is withdrawn in view of Applicants appropriate amendments to claims filed in the Applicants response of 10/30/2008.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4 stand rejected under 35 USC 102 (b) as being anticipated by Amaar et al (2002, J. Biol. Chem. 277:12503-12059) for the reasons of record set forth in the office action mailed on 04/30/008.

The above claims are directed to a method of identifying compounds that promote the capability of osteoblasts to form extracellular matrix in vivo by measuring the increase in the levels of FHL2 protein or FHL2 gene expression in osteoblast cells in vitro.

Response to Applicants arguments of 10/30/2008:

Applicant amends the claims and argues that the instant invention is not anticipated by Amar reference because Amar fails to show expression in osteoblasts in situ and only describes FHL2 expression in cells lines in vitro.

The applicants arguments are however, found not persuasive because the instant claims still read on the same in vitro method steps of increasing the expression of FHL2 protein expression by contacting an osteoblast cell in vitro with a compound. Amar clearly discloses increasing expression of FHL2 in vitro by retroviral vector mediated expression of FHL2 cDNA. Thus Amar clearly anticipates the invention as claimed. Hence the rejection is maintained.

Claims 1-5 are rejected under 35 USC 102 (b) as being anticipated by Lai et al (2002, J. Bone and Mineral Res. Vol.17; supp (1), pp. S129; art of record) for the reasons of record set forth in the office action mailed on 04/30/008.

The above claims are directed to a method of identifying compounds that promote the capability of osteoblasts to form extracellular matrix in vivo by measuring the increase in the levels of FHL2 protein or FHL2 gene expression in osteoblast cells in vitro and further FHL2 interacts with Runx2 protein in cells.

Response to Applicants arguments of 10/30/2008:

Applicant amends the claims and argues that the instant invention is not anticipated by Lai reference because Lai fails to show expression in osteoblasts in situ and only describes FHL2 expression in cells lines in vitro.

The applicants arguments are however, found not persuasive because the instant claims still read on the same in vitro method steps of increasing the expression of FHL2

protein expression by contacting an osteoblast cell in vitro with a compound. Lai clearly discloses increasing expression of FHL2 in vitro by a vector mediated expression of FHL2 cDNA. Lai further teaches Fhl2 expression is up regulated in these cells which further show an cell proliferation, matrix mineralization, osteocalcin up regulation and Runx2 (Cbfa1) up regulation. Thus Lai clearly anticipates the invention as claimed. Hence the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-6 are rejected under 35 USC 103 (a) as being unpatentable over Lai et al (2002, J. Bone and Mineral Res. Vol.17; supp (1), pp. S129; art of record) in view of Amaar et al (2002, J. Biol. Chem. 277:12503-12059; art of record) in view of Muller et al (2002, The EMBO Journal 21:736-748; art of record).

The above claims are directed to a method of identifying compounds that promote the capability of osteoblasts to form extracellular matrix in vivo by measuring the increase in the levels of FHL2 protein or FHL2 gene expression in osteoblast cells in vitro and further FHL2 interacts with Runx2 protein in cells.

Regarding the claims 1-5 Lai teaches over expressing FHL2 gene and protein in osteoblasts (MC3T3-E1) in vitro by contacting FHL2 cDNA (a compound) cloned in a expression vector (Abstract). Lai further teaches Fhl2 expression is up regulated in these cells which further show an cell proliferation, matrix mineralization, osteocalcin up regulation and Runx2 (Cbfa1) up regulation. Regarding claim 6 RunX2 is well known in the art, at the time of invention, as a transcriptional factor involved in the expression of osteocalcin. Lai further teaches that FHL2 may play an important role in bone formation. Lai however, does not teach determining the level of interaction between Fhl2 protein and Runx2 protein in the osteoblast.

Regarding the claims 1-4 Amaar teaches over expressing FHL2 gene and protein in bone cells (U2 osteoblasts or osteosarcoma cells) in vitro by contacting FHL2 cDNA (a

compound) cloned in retroviral expression vector (p.12054, col.2, paragraph 8 bridging p.1205; p.12059, col.1, paragraphs 3-5 bridging col.2). Regarding claim 6 Amaar teaches that Fhl2 is strongly localized in the nucleus.

Muller teaches Fhl2 is transcriptional co-activator (entire article; Abstract; p.746, col.2 , 2nd paragraph).

Thus it would have been obvious to one of skill in the art to try to establish the mechanism of interaction between Fhl2 and Runx2 proteins in the method of Lai as Amaar teaches the nuclear localization and Muller teaches its involvement in transcriptional activation. One of skill in the art would have motivated to try to establish physical interaction between Fhl2 and Runx2 as they both are transcriptional activators and both seem to localize and act in parallel in the expression of proteins involved in upregulation of osteocalcin in osteoblasts. One of skill in the art would have a reasonable expectation of success in establishing the protein interaction between Fhl2 and Runx2 as the art teaches that these proteins have protein interaction domains and further the art teaches the routine method of determining physical interactions using readily available immuno co-precipitation techniques of the interacting proteins. Thus the invention was prima facie obvious to the Artisan at the time of invention.

Conclusion

No claim allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any


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extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanne Ph.D.*, whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Thursday from 9 AM-7PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach Ph.D.*, may be reached at **(571) 272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

/Robert M Kelly/

Primary Examiner, Art Unit 1633

<i>Application Number</i> 	Application/Control No.	Applicant(s)/Patent under Reexamination	
	10/561,902	SCHULE ET AL.	
	Examiner KELAGINAMANE T. HIRIYANNA	Art Unit 1633	